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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,125	02/21/2006	Andrew Chee-Yuen Chan	11669.0150USW2	2225

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EXAMINER	
LI, QIAN JANICE	

ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/538,125	CHAN ET AL.	
	Examiner	Art Unit	
	Q. Janice Li, M.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10,11,13 and 16-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-6,8,10,13 and 16-23* is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☒ Claim(s) *7,11,18 and 24-28* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment and remarks submitted on November 6, 2007 are acknowledged. Claims 9, 12, 14, 15 have been canceled. Claims 1-8, 10, 13, 16, 17 have been amended. Claims 18-28 are newly submitted. Claims 1-8, 10, 11, 13, 16-28 are pending and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated.

Priority

The priority claims to U.S. provisional applications 60/434,115 or 60/476,481 are acknowledged in view of persuasive arguments.

Claim Objections

Claim 7 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 7 depends from claim 6 and has the same scope as claim 6, because they both drawn to a mouse genome contains a disruption in the endogenous CD20 gene. Further, a mouse could not have an endogenous murine CD20 gene. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 11 is objected to because the phrase "B lymphocytes and /or pre-B" should be inserted after "said".

Claim 18 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 18 depends from claim 2, and has the same scope as claim 2. This is because the specification defines the "endogenous promoter" as "*The term 'human endogenous promoter' refers to the promoter that is naturally associated with the polynucleotide sequence that encodes the human protein that is to be introduced into the animal to form a transgenic animal*". As such the human endogenous promoter of claim 2 is the same as the human CD20 promoter recited in claim 18. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claims 24-28 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 8, 10, 11, 20, 21, respectively. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). In the instant case, both sets of claims are directed to a method where the numbers of B cells or pre-B cells are compared at before and after administering an agent, while the first set of claims set forth explicitly the method steps.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8, 10, 11, 13, 16-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Wadsworth et al.* (USP 5,720,936), in view of *Countouriotis et al.* (Stem Cells 2002:20:215-229), and *Capecchi et al.* (US 5,627,059).

Wadsworth et al. teaches making a transgenic mouse whose genome comprises a nucleotide encoding a human gene (APP) known to be associated with a disease (Alzheimer's) operably linked to a human APP promoter (e.g. column 3, lines 34-38), and using such for screening compounds capable of affecting the disease gene product APP peptides (e.g. the abstract and claims). Although *Wadsworth et al.* teaches a different mouse model expressing different disease genes, it establishes the need (motive) and the state of the art pertaining to making a transgenic mouse expressing a human disease gene and using such animal for drug screening.

Countouriotis et al. supplements *Wadsworth et al.* by establishing it was well known in the art at the time of instant priority date, the association between CD20 and B cell lymphoma. *Countouriotis et al.* teaches certain cell surface antigens, such as CD20 have been used as molecular drug targets in the treatment of hematological

malignancies, such as lymphomas (e.g. the section starting page 216). *Countouriotis et al.* teaches CD20 is expressed on pre-B cells, mature B cells, and up to 95% of B-cell non-Hodgkin's lymphoma, but is absent from stem cells and plasma cells, and hence suitable as a drug target for the treatment of NHL. Based on such knowledge, a drug named Rituimab had been developed, which is a chimeric murine/human anti-CD20 mAb. Binding between the anti-CD20 antibody and CD20 on B-lymphocytes cells would lead to killing of the cells (decrease in number). *Countouriotis et al.* further discusses clinical efficacy of using such antibody drug for the treatment/retreatment of NHL. Apparently, Rituximab had become the most widely studied and available therapeutic mAbs for the treatment, but still far from ideal. Hence, there is a need for developing other drugs capable of more effectively targeting CD20, and thus a need for a model in screening and testing compounds targeting CD20.

Capecchi et al. supplements the teaching of *Wadsworth et al.* in view of *Countouriotis et al.* by illustrating the general state of the art on making a transgenic mouse, the process and necessary tools for targeted insertion/disruption of a transgene of interest (e.g. column 5). *Capecchi* et al. teaches a vector for producing knockin/knockout mice. Particularly, that the vector has a first and second homologous DNA sequence, and a positive selection marker between the two homologous sequences. See Figure 1. Furthermore, *Capecchi* et al. teaches various markers that can be used in these vectors. See Table I, col. 7-8. *Capecchi* et al. teaches that these vectors can then be used to produce transgenic animals, wherein ES cells are the preferred target cells (see paragraph bridging col. 15-16), wherein the vector can then

be introduced into the ES cells by electroporation or microinjection. These transformed ES cells can be combined with a blastocysts and then grown and contribute to the germ line of the resulting chimeric animal. *Capecchi.* establishes that these vectors and methods can be used to create a transgenic mouse of interest useful for drug screening.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teaching of *Wadsworth et al.* in view of *Countouriotis et al.* and *Capecchi et al.*, by making a transgenic mouse expressing CD20 and using such for drug screening with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because the need for developing a more effective drug for treating NHL as taught by *Countouriotis et al.* Given the state of the art in making a transgenic mouse as taught by *Wadsworth et al.*, and *Capecchi* et al. one would have had a reasonable expectation of success in making the CD20 transgenic mouse and using such for drug compound screening. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is **571-272-0730**. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The **fax** numbers for the organization where this application or proceeding is assigned are **571-273-8300**. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

For all other customer support, please call the USPTO Call Center (UCC) at **800-786-9199**.

Q. JANICE LI, M.D.
PRIMARY EXAMINER

Q. Janice Li, M.D.
Primary Examiner
Art Unit 1633

QL
January 17, 2008